

## Intramuscular Poly-ICLC in HIV Infection: Preliminary Finding

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Poly-ICLC (PICLC) induces interferons alpha and beta, other cytokines, and corticosteroids, and at low doses only it activates NK cells, macrophage/monocytes, and specific cytotoxic T cells. It is also a co-factor for the 2'-5' oligoadenylate system mediating the antiviral action of the interferons; this pathway is inhibited by the HIV.

In an open pilot trial, low-dose (2-6 mg) PICLC was administered intramuscularly (IM) weekly and then bimonthly with or without zidovudine over 10-14 months to 13 HIV patients in Walter Reed Stages 4-6. PICLC was well tolerated, with no significant clinical or laboratory toxicity. Side effects consisted of a 12- to 24-hour flu-like syndrome with low-grade fever and malaise. On weekly dosing, 12/13

patients remained clinically stable, and most reported an weight gain, improvement in fatigue, and other constitutional symptoms. T<sub>4</sub> counts remained unchanged or rose in 8/9 patients, and cultures were negative at 4 months in 5/9. However, 5 patients since deteriorated on a bimonthly regimen; 4 have died, 3 after discontinuing treatment altogether. HIV cultures and serum P-24 again became positive. At 14 months, dosing was changed to 1 n biweekly. Preliminary clinical and laboratory results releva safety and toxicity at 20 months of administration will be prese IM PICLC can be safely administered to HIV-infected patients weekly basis.

## Embryonic Human Neurons, Astrocytes, and Microglial Cells Are Resistant to HIV-1 In Vitro but Are Destroyed by Infected Monocytes

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Neuropathological studies have suggested that HIV-1-infected cells within the brain are from macrophage-monocyte lineage. To better understand the interaction of HIV-1 with CNS cells, we used an *in vitro* approach.

Spinal cord cultures were obtained from 8- to 12-week-old human embryos and contained neurofilament + neuronal cells, astrocytes (60% of GFAP +, Dr +, CD4 - cells), and microglial cells (5%) which were subsequently isolated. Cells, in microglia-enriched cultures, contained esterase activity (85% +), phagocytized zymosan particles (90% +), and expressed several (KiM7, OKM1, Fc) but not all the antigenic markers expressed on freshly isolated monocytes (which are also Dr, Kim6, LeuM3, LeuM5, EBM11 strongly positive). Neurons, astrocytes, rested microglial cells, as well as LPS, IFN-stimulated microglial cells were resistant to HIV-1 infection as judged by RT activity in supernatant, p24 antigen detection, *in situ* hybridization.

On the other hand, when infected U937 cells (a continuous mono-macrophage cell line) were co-cultured with uninfected spinal cultures, astrocytic lesions were induced which were not obse after co-culture with infected lymphocytes, uninfected U937 TNF-, LPS, IFN-stimulated U937. An adherence of U937 to acytes was required to induce lesions. Finally, in HIV-1-infected human brain, p24 containing cells have a pattern of antigenic mar similar to that of monocytes.

In conclusion: (1) Human microglial cells can be isolated and different antigenic markers than monocytes; (2) they are resistar HIV-1; (3) astrocytes which are also resistant to HIV-1 can be destroyed after contact with infected monocytic cells; (4) most HI infected cells within brain seem to be monocytes and not resic microglial cells.

## Subacute Encephalomyopathy Associated with HTLV-I: Pseudobulbar Paralysis and Mental Deterioration

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Progressive spastic paraparesis associated with human T-lymphotropic virus type I (HTLV-I) infection has been reported in Caucasian patients living in the non-tropical metropolitan area of Santiago, Chile. We describe a 51-year-old mestizo woman living in the same area, who presented in March 1987 with progressive dysarthria, dysphagia, and involuntary crying and laughter. Physical examination showed hyperreflexia, extensor plantar responses, and minimal spastic gait. Blood biochemical laboratory analyses as well as brain CT, EEG, EMG, and trimodal evoked potentials studies were initially normal. Cerebrospinal fluid analysis showed mononuclear pleocytosis (25/ $\mu$ l) with an IgG index of 0.92. Clinical evaluation

conducted 18 months later revealed important mental deteriorat with anarthria and tetraparesis. Tibial nerve somatosensory evol potentials study disclosed absence of cortical response. The pati had IgG antibodies to HTLV-I in serum and CSF using ELISA (1:1 and 1:20 respectively) and Western immunoblot. Virus isolation fr cocultivated peripheral blood lymphocytes was conducted using immunoblot techniques, electron microscopy, and DNA genomic amplification. Therapy with corticosteroids and AZT did not modify clinical course. Pseudobulbar paralysis must be considered in spectrum of neurological diseases associated with HTLV-I.

## Progressive Myelopathy in a Californian Infected with Human T-cell Leukemia Virus

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HTLV-I virus is associated with a chronic progressive myelopathy known as tropical spastic paraparesis (TSP) in the Caribbean and HAM (HTLV-I-associated myelopathy) in Japan. This virus has low seroprevalence (~ 0.01%) in the USA. A man, age 45, presented with a year of progressive leg numbness, weakness, and bowel, bladder, and erectile dysfunction. He used intravenous drugs, lived since birth in California, and was of Mexican ancestry. Examination showed isolated thoracic myelopathy, with leg spasticity, decreased vibration and position sense, hyperreflexia, clonus, and Babinski signs. Spine MRI, brain CT, NCV, B<sub>12</sub>, SPEP, and syphilis studies

were all normal. CSF exhibited 5 WBC/mm<sup>3</sup>, increased protein a IgG (94 and 18 mg/dl), and two oligoclonal bands. High titers HTLV-I/II antibody were demonstrated in serum and CSF by RIP IFA, and Western blot tests (HTLV-I p19, 24, 46, 55 bands). Antib and antigen tests for HIV were repeatedly negative. HTLV-II is m frequent in Californian IVDA, yet without reported disease correla Most antibody techniques are unable to resolve between HTLV-I a -II, but PCR, and anti-HTLV-I-unique recombinant protein tests a in progress. Exposure parenterally is presumably responsible for th rare case of HTLV myelopathy in the USA outside the Southeast.